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SOME IMMUNOBIOLOGICAL CHANGES IN RECRUIT PERSONNEL DURING THE E--ETC(U)
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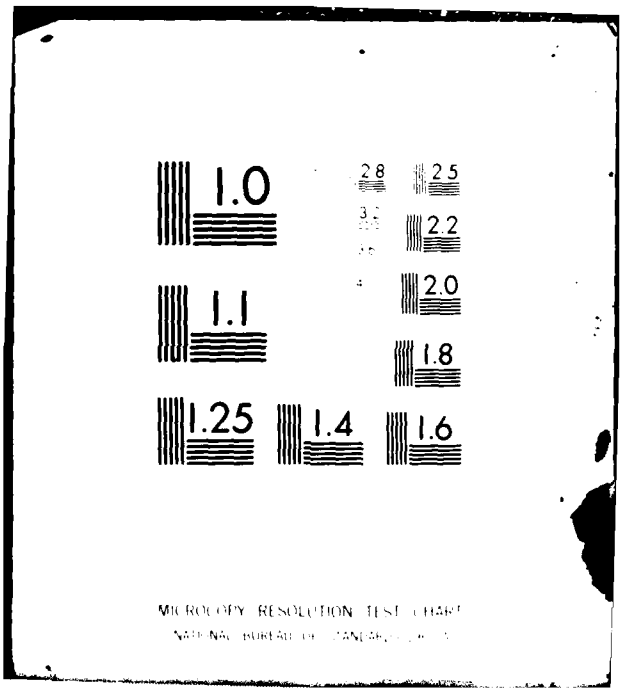
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SOME IMMUNOBIOLOGICAL CHANGES IN RECRUIT PERSONNEL DURING THE EARLY PHASE OF RECRUIT TRAINING

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SOME IMMUNOBIOLOGICAL CHANGES IN RECRUIT PERSONNEL DURING THE EARLY PHASE OF RECRUIT TRAINING

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SUMMARY

Acute respiratory disease (ARD) is a major problem in the military, particularly among recruits, where the prevalence of ARD is high during the first few weeks of recruit training. This clustering of ARD early in recruit training supports the hypothesis of infection from a common source. Incoming Navy recruits go to a central processing area and this contact could allow the spread of a large variety of infectious agents among individuals who have come from all areas of the U.S. Intensive studies to isolate infectious agents (both bacterial and viral) from Navy recruits with ARD resulted in identification of a causative agent in approximately one-half of these symptomatic recruits.

Our study evaluated lymphocyte transformation and response to skin test antigens during the first 15 days of recruit training. The data revealed a decreased 24 hour reaction to skin test antigens from Day 1-5 of recruit training. Response to skin test antigens were normal from Day 9-15 of training. Lymphocyte transformation remained normal through Days 1-5 but significantly decreased as illness scores increased.

This impairment of the immune system may play a role in the recruits' increased susceptibility to ARD. The possible relationship between the moderate decrease in immune competence and the stress the individual experiences during the transformation from civilian to military environment requires further study.

The high incidence of respiratory infections during the early phase of recruit training has been observed in both war and peace time training of military personnel (1,2,3,4,5). This seems to have a clear explanation in that young men and women are brought together from different parts of the country, exposing each other to a variety of microbial agents against which they had either natural or acquired resistance. This concept of the infection process carries with it the assumption that resistance to the infectious agents within and around us is mediated by immune mechanisms. Therefore, any specific antibody deficiency will lead to an increase in susceptibility to those infectious agents for which immunity is lacking. The assumption that immune mechanisms are responsible for susceptibility (or resistance) to infectious agents is validated by experiments of nature (immune deficiency disorders) (6,7) and observed in experimental studies in animals and man as a result of spontaneous or induced immune deficiencies (8,9,10).

In studying respiratory infections in a recruit population, nearly one-half of recruits reporting with respiratory complaints were found to be "free" of any (identifiable) causative agent (3). These data suggest factors other than the acquisition of (recognizable) microbial agents as cause/effect. This lack of a causative agent raises a question as to other causes of respiratory complaints in a population that appears to be free of disease producing agents widely recognized as associated with respiratory illness. It is possible that either a new agent or agents are responsible for the illnesses. Alternatively, organisms of low virulence which are not normally associated with clinical disease may become pathogenic (opportunistic pathogens) to a human host at a time when the host is experiencing impaired resistance. Thus the laboratory fails to identify other than normal flora lending to the mystery of the cause(s) of these illness episodes. It has been shown many times in animals and humans (11, 12, 13) that "stress" markedly increases susceptibility. Whether adaptation stress plays a role in recruit illnesses is yet to be proven, although it is an attractive hypothesis (14).

The present study was an effort to determine some of the biological mechanisms which might lead to a better understanding of the high degree of recruit susceptibility to respiratory illnesses in the early phase of recruit training. The data suggests a sluggish antigen recognition system during the first 5 days of training as demonstrated by a tempered response in cell mediated immune reactions.

MATERIALS AND METHODS

Men arrived daily at the Navy Recruit Training Center in Great Lakes, Illinois.

The first phase of this study was to determine daily leukocyte blood counts on 30 recruits from a single company for the first 10 days after reporting for recruit training and again at day 28. This pilot study was made to obtain a base line leukocyte count over the period of time during which "exposure" to various infectious agents might occur due to the intermix during recruit processing and company formation.

The second phase of the study spanned a period of 7 weeks. Eight recruit companies made up the study population. Each company was made up of from 70-90 men. Study companies were randomly selected with a bias toward selecting a company either Monday through Wednesday so that 72 hour interviews could be held without weekend interference. A study "company day" was initiated at alternate days of training from day 1 through day 15 (with a study company at any given training day studied considered to be "representative" of the physiological/psychological/illnesses experienced during early recruit training). Each man of the study company was interviewed regarding upper/lower respiratory complaints (cough, sore throat, nasal discharge, congestion, headache, effects on speaking voice), past history of frequent upper respiratory infections (URI), present or history of "athletes foot", history of mumps, boils, or allergies.

Sampling: Approximately 5 cc of blood was collected from each company member in a B-D vacutainer

containing 0.4 ml of 15% EDTA for total leukocyte and differential leukocyte count. Also, 10 persons from each company were randomly selected for lymphocyte transformation (LT) studies (15). From these individuals an additional 20 ml of blood was obtained in a vacutainer with heparin. Oral temperatures were also taken at this time.

Leukocyte Counts: Leukocyte counts were made in duplicate in a Coulter Counter (Model F) and differential counts were made after Wright staining.

Skin Testing: To determine the status of delayed hypersensitivity reactivity, 4 antigen preparations were given intradermally. Mumps and mumps placebo were purchased from Eli Lilly & Co., candida and trichophyton antigens (Hollister-Stier Laboratories). Candida was used diluted 1:100 and trichophyton was used diluted 1:50, 0.1 ml of each antigen preparation was administered to each volunteer in a random pattern on the volar aspect of the left forearm. The pattern was randomized by computer and after the antigens were given, no one knew the pattern that might have been given to any individual. Observation and measurement of the reactions (erythema and induration) were made at 24 and 48 hours. A medical questionnaire was completed and temperatures taken at these intervals.

Interpretation of Skin Test: Reaction to mumps skin test antigen (induration) of 0 through 7 mm were considered negative, 8 and above were considered positive. Induration due to candida or tricophyton testing was recorded as measured.

Illness Scores: Health Status interview cards were administered and weighted as follows:

Temperature	3 points
Sore Throat	1 point
Cough	1 point
Productive Cough	2 points
Coryza	1 point
Headache	1 point
Abnormal Voice Tone	1 point

RESULTS

The results of the daily WBC counts of 30 men for the first 11 days and again for day 28 of recruit training are shown in Fig. 1. While the average count at the earliest stage of recruit training

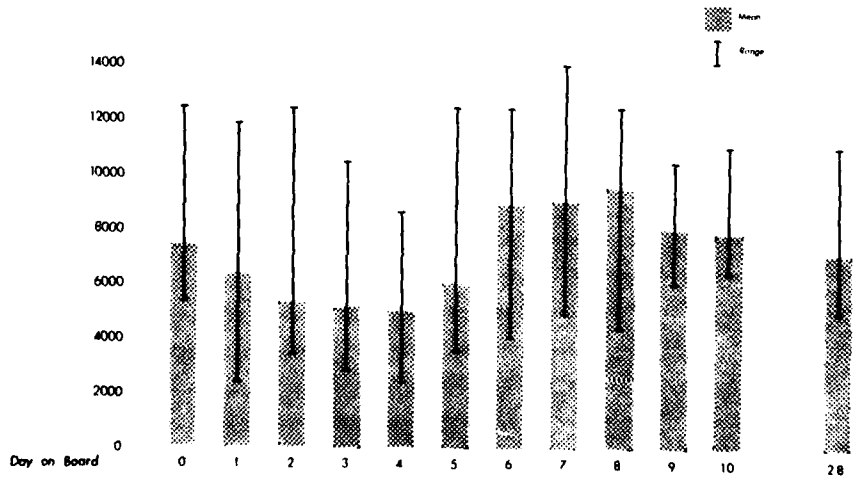

FIGURE 1

Total mean leukocyte count of 30 recruits in early phase of recruit training.

(day 1) averaged 7,200/mm^3 (range 5400-12,400), there appears a precipitous fall by day 2 through day 6. The average count at day 2 was 5200 (range 2499-8600). Nine of the 30 men (30%) had a count of less than 4000/mm^3 by day 3 of testing. This modest leukopenia remained for 4 days, after which the average count "rebounded" to above the original average count and then to near the initial count by day 10.

The illness score data for the 8 companies studied are shown in Fig. 2. While approximately 15% of the men reported to recruit camp with URI, it can be seen that these symptoms increase in severity after the first week of training and may not have maximized by the end of our study (15th day of training).

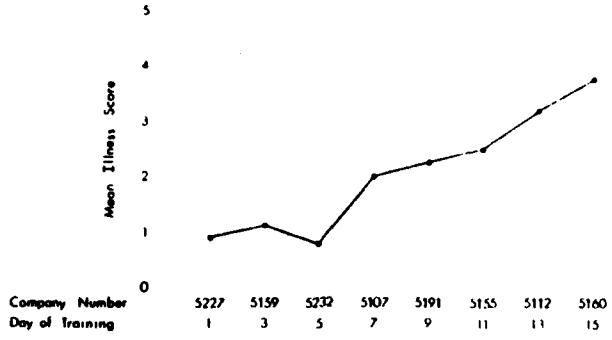

FIGURE 2

Illness scores of recruits by day of training

The skin test response to mumps antigen at 24 and 48 hours is shown in Fig. 3 and 4. As shown, the men making up the companies during day 1,3, and 5 days of training showed a significantly smaller reaction (enduration) ($p = < 0.01$) at the 24 hour reading compared to those in companies that were tested at the 7th through the 15th day of training. However, as shown in Fig. 3, the recruits in the

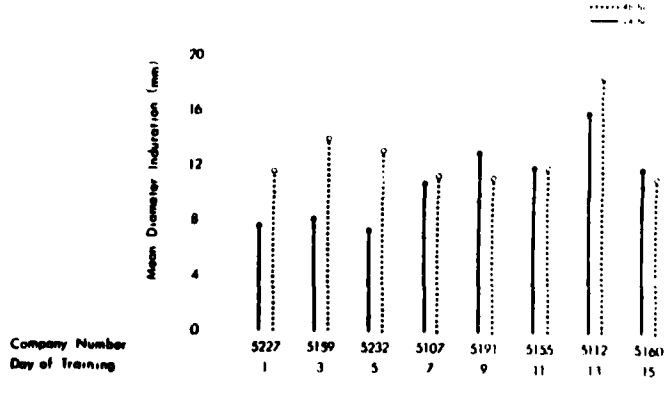

FIGURE 3

A comparison of the responses to mumps skin test antigen at 24 and 48 hrs. Readings for days 1-5 at the 24 hr period are significantly different than the readings at days 7-15.

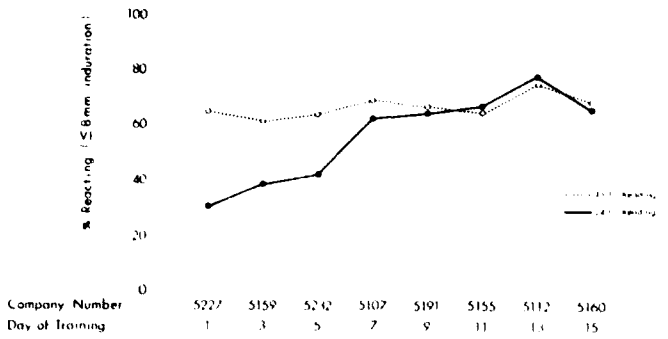

FIGURE 4

Percent of test subjects reacting to mumps skin test antigen by day of training.

1-5 day companies showed a reaction equal to the recruits from the 7-15 day companies at the 48 hour reading. This suggests that the immune system of these individuals was under some state of depression or that the immune system did not easily recognize an antigen which was recognized by those recruits tested from 7-15 days of training within the 24 hour time frame. This is supported by the data in Fig. 4 comparing the percent of men reacting to mumps skin test antigen at 24 and 48 hours. This reduced response for the 24 hr reading during the first 5 days of recruit training was also observed for the antigens candida and trichophyton.

To determine if the difference seen in skin reactivity was due to the health status of recruits (illness score vs. skin reactivity), men without illness scores (score of 3 or less) and men with illness scores (score of 4 or more) in companies 5159 (day 3) and 5160 (day 15) were compared. Analysis was made by dividing the size of induration into 3 groups; 0-7 mm; 8-17 mm; and > 17 mm (Table I). The difference between the day 3 trainees and day 15 trainees was highly significant ($P = < 0.001$). Note that the company 5159 was heavily weighted in the smaller size (<7 mm) reaction size group. While the numbers were small, the data suggest that a recruit in the early phase of training did not recognize or respond to an antigen to the degree that a recruit responds after the first week of training. To test the effect of "illness" vs "well" on the response to mumps skin testing, we compared the reactions of those recruits who were considered "ill" to those who were considered "well" for each of the test days. This comparison is shown in Fig. 5. It is clear from this data that the reduced skin reactivity observed in early training can not be attributed to an ongoing illness episode.

The data from the LT study made on the randomly selected 10 men from each company are shown in Fig. 6. The men in the early stages of training had a significantly higher LT response when stimulated with phytohemagglutinin than the men from days 11 to 15 ($p = < 0.01$). The early training LT response was similar to the response of two normal controls used throughout the study. The reduced LT level of transformation in the training period from 7-15 days has an inverse relationship to the illness scores (Fig. 2). This suggests that the (imparied) recognition of antigen from days 1-5 was not due to a compromised lymphocyte blastogenesis capability as judged by their lymphocyte response to phytohemagglutinin. The data shows a reduced blastogenesis after day 7 which corresponds to the increasing evidence of illness in the population shown by the illness scores (Fig. 2).

TABLE I

24 hour Induration Reading

"Sick" Recruits

Induration		Day 3 Company Number 5159	Day 13 5160
0-7 mm	observed	8	10
	expected	4.5	13.5
8-17mm	observed	2	19
	expected	5.25	15.75
>17mm	observed	0	1
	expected	0.25	0.75

$X^2 = 6.6454$ P= 0.03

"Well" Recruits

0-7 mm	observed	61	17
	expected	48.91	29.02
8-17mm	observed	8	22
	expected	18.8	11.16
>17mm	observed	0	2
	expected	1.25	0.74

$X^2 = 28.096$ P= <0.001

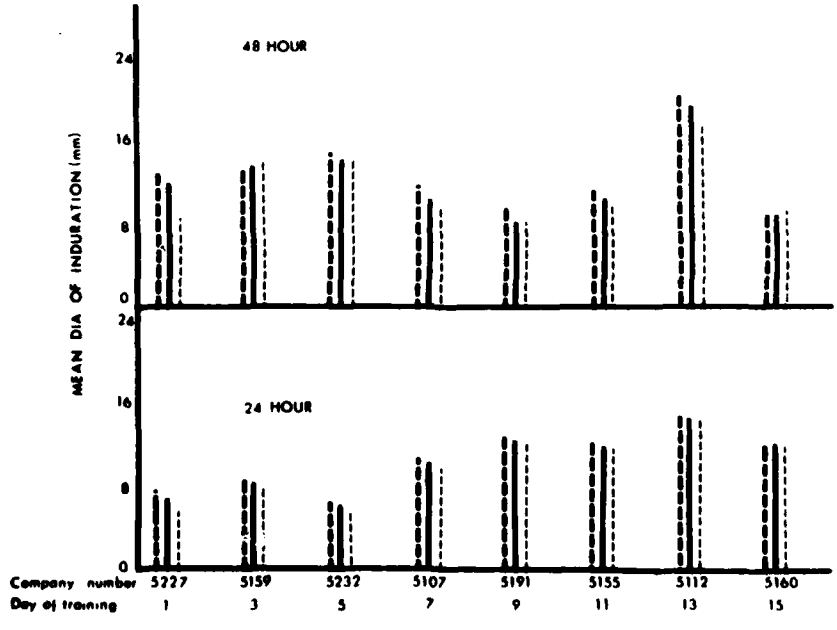

FIGURE 5

A comparison of skin tests to mumps antigen between men who were ill (- - - - -), well (•——•) and both ill/well (————).

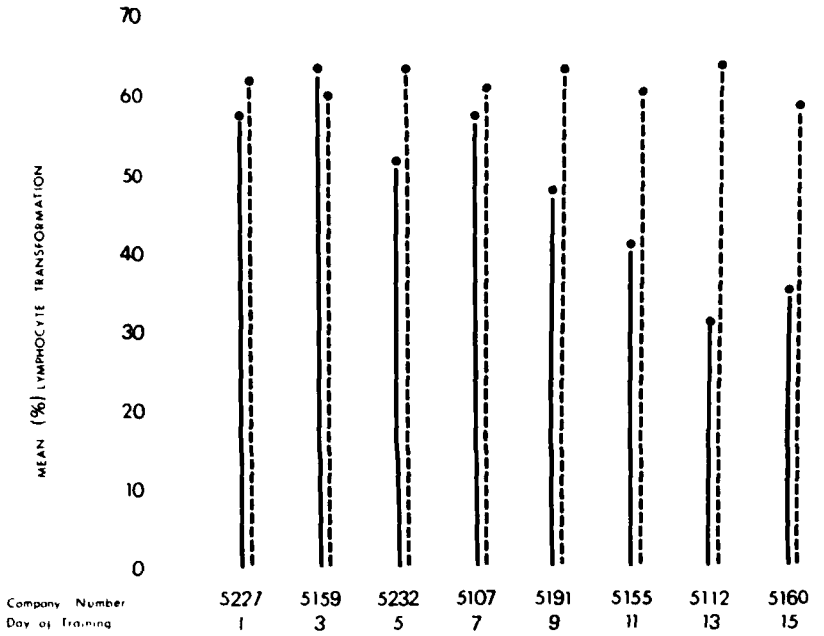

FIGURE 6

Lymphocyte transformation response to phytohemagglutinin stimulus of 10 men from each company studies (——) compared to normal controls (•——•).

DISCUSSION

In recent years, increasing interest has been shown in the effect of stress on illness (12,16,17). The experiments in the NASA Skylab Program demonstrated depression of lymphocyte transformation and rosette formation on the day of splashdown (18). Retrospective investigations of bereavement and other severely stressful situations have been claimed to show an association between stress and many diseases (19,20). In a prospective study on the behavioral, endocrinological and immunological consequences of bereavement, it was found that lymphocyte blastogenesis in response to phytohemagglutinin was significantly depressed two weeks after bereavement (21). Viral infections and immunizations have also been shown to suppress cell mediated immunity in humans (22,23,24,25,26). Von Pirquet observed that children lost their skin reactivity to tuberculin a few days prior to the exanthem of measles, with a gradual return to positive reactions 5-10 days after the rash subsided (27).

The purpose of the present study was to better understand the reason(s) for the excess amount of illness seen in early recruit training. The question of whether causes other than microbial, such as a reduced immunocompetence, as a consequence of the requirements of adaptation to the new social environment of recruit training, may play an important role in URI is an intriguing one. If the illness observed in early recruit training was a cause/effect of the spread of microbial agents, there should have been a seasonal or epidemic pattern to the morbidity seen. Except for influenza epidemics, such patterns were seldom observed. There appeared a uniform excess of respiratory illnesses during the first 3 weeks of recruit training, winter or summer. This suggests that other factor(s) may be important in the recruit becoming ill early in training. The (impaired) immune response, as suggested by the retarded skin responses to the 3 antigens administered during this study, may be a "permissive factor" for the high incidence of respiratory complaints, or to increased susceptibility to "normal flora" in the early stages of recruit training since only about 50% of the respiratory infections

could be associated with a known disease producing agent. Differential examinations of blood smears failed to reveal significant alterations in leukocyte (lymphocyte/neutrophil) proportions either prior to recruit training, during the first 5 days of recruit training, or after the leukocyte count returned to a normal range. However, the moderate leucopenia observed during the first 5 days of recruit training suggests an alteration in this homeostasis network.

It has been reported that psychologically vulnerable individuals are more likely to seek medical attention than those judged non-vulnerable (28). It would appear from our observations that the response to "stress' in the early days of recruit training may increase susceptibility (vulnerability) because of the immuno-depressed state that our study indicates, which may become the predisposing factor to excess URI episodes seen in recruit populations. This study gives additional support to the hypothesis that alterations in social situations and the coping process may have a direct effect upon susceptibility. The concept that psychosocial factors may be predisposing for an individual to become ill (13,28), our data and that of others (29), suggest that one of the events of this predisposition may be a depressed immunocompetence.

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Lymphocyte transformation and response to skin test antigens in Navy recruits were studied during the first 15 days of training to determine if there were significant changes in immune competence which could account for the high prevalance of ARD. Decreased response to skin test antigens at 24 hours was noted during the first 5 days. This response was normal from Day 9-15. In contrast, lymphocyte transformation was normal during the first 5 days but decreased significantly as illness scores increased. This documented decrease in immune response may be due to the stress factors involved in the transition from a civilian to a military environment.

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